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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/142,660	12/23/1998	RAINER HINTSCHE	60953/119	2492

7590 01/15/2002

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1655	35

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/142,660	HINTSCHE ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 17 December 2001 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *21-55 and 58-60*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit: 1655

Continuation of 5. does NOT place the application in condition for allowance because: Agreement is reached where at page 2 of the response it is asserted that the spacing between the electrode structures is less than 3 micrometers (claims 21-55 and 58-60) and can also be less than 1 micrometer (claim 61). The claims do not, however, place a lower limit on the gap between the electrode structures. Consequently, the claims read of gaps being but fractions of Angstroms. In contrast, page 5, line 12, of the specification teaches that the invention has been found to be functional where the gap is a "few nm from one another." Given that one nm is equal to 10 Angstroms, the specification does not enable the manufacture and use of electrode structures where the gap is less than 3 or 4 nm, or 30 to 40 Angstroms

Argument is presented that the Office actions "do not list any credible, objective evidence to cast doubt on the claims' presumption of validity" (response at page 3). This argument ahs been fully considered and has not been found persuasive. As acknowledged by applicant, the Office action does present a Wands analysis of the claims in light of the specification. As set forth at page 4 of the Office action of 18 September 2001, the specification does not set forth sufficient guidance so to enable one of skill in the relevant art, at the time the invention was made, so to adapt the disclosure whereby any molecule or molecular complex can be detected in any diluent. It is without question that the method is directed to the area of chemical reactions, including those chemical reactions and chemical complexes found in and resulting from physiological activity, areas of art that have been recognized as being unpredictable. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

Agreement is reached in the specification needed not set forth in detail, be it by example or otherwise, every possible permutation encompassed by the claims. The disclosure does, however, need to set forth in sufficient detail disclosure that is sufficient so to enable the full scope of the claims, not just one small area encompassed therein.
At page 4 of the response attention is directed to US Patent 5,200,313 as being exemplary that greater disclosure is not needed. While agreement is reached in that perhaps not all hybridization reactions are unpredictable, the very nature of applicant's argument implies, however, that some of the reactions are unpredictable. The claimed invention, however, is not limited to just "predictable" hybridization reactions, but encompasses all hybridization reactions, as well as all other compounds, be they organic (e.g., steroids, enzymes, metabolic products, carbohydrates, complexes, etc.) as well as inorganic compounds. In view of the breadth of scope, the claimed invention has not been found to be fully enabled by the disclosure.

At pages 5 through 10 argument is presented in that the declarations of (1) Dr. Rainer Hintsche and Dr. Manfred Paeschke (signed December 2000); and (2) Dr. Rainer Hintsche (signed August 9, 2001) have not been properly considered by the Office. Upon further review of the declaration of both Dr. Rainer Hintsche and Dr. Manfred Paeschke, it is noted again that both declarants are co-inventors of the instant application and as such do not necessarily present the opinion of a disinterested third person. The declaration states that they have proven in 1998 that the device made in accordance with the disclosure was able "to detect DNA hybridization and differences between 'full-matching,' 'mismatching,' and 'no matching' and oligonucleotides using 24-mer oligonucleotide sequences as probes." Argument is also presented that in Example 3 of a journal published in 2000 that they were able to detect tumor marking agent cytokeratin 20 complexed to a respective catching oligonucleotide without undue burden. These arguments have been fully considered and have not been found to be persuasive towards the withdrawal of the rejection as the claimed method is not limited to the detection of only the interaction or binding of DNA to oligonucleotides. In short, applicant is arguing enablement for a specific species encompassed by the claims when the claims are not so limited. As indicated above, the specification must fully enable the entire scope of the claims. It is further noted that declarants direct attention to Appendices 1 to 8. A review of the instant declaration as well as the earlier version of same which was submitted with the signature of only Dr. Hintsche (signed December 11, 2000; Paper No. 16) have not been found to contain the aforementioned appendices. Accordingly, it is not possible to compare the particulars of just how the referenced methods align with the instant disclosure.

The declaration of Dr. Hintsche, received 28 August 2001, signed 09 August 2001 (Paper No. 29) has again been fully considered and has not been found persuasive towards the withdrawal of the rejection of claims under 35 USC 112, first paragraph. As previously indicated, the declaration is that of co-inventor and as such does not represent the opinion of a disinterested third party. The declaration has been found to set forth four examples. Example 1 being directed to detection of tumor marker CK-20 DNA; Example 2, detection of FLAG antibody using impedance measurement; and Examples 3 and 4: similar to examples 1 and 2 but employ simultaneous electrode processes in addition to impedance measurement. Upon review of Example 1, it is noted that the electrode had a width of 1 micrometer and had spacing of 0.7 micrometer, in Examples 2 and 4 the electrodes had a width of 2 micrometer and spacing of 0.8 micrometer; and Example 3 were spaced 0.8 micrometer; and in Example 3 the electrodes had a width of 1 micrometer and were spaced 0.7 micrometer. These are critical limitations not present in the claims. Furthermore, the examples are directed to either hybridization reactions of antigen-antibody interactions where the target and probe are in a purified state. The claims are not so limited. As indicated above, the claims have been interpreted as encompassing the detection of virtually any molecule or molecular complex, no matter how large or how small, how heterogeneous the assay sample may be or whether the assay is to be part of a physiological system or part of some chemical reaction. While applicants'/declarants' argument may have greater weight if the claims were so limited to hybridization and immunological reactions that parallel the disclosure, such is not the case. It is further noted that the specification states at page 5, lines 13-20 that the electrodes must be insulated from one another. Such an admitted critical limitation of the operational condition is not recited in the claims.

For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.